(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/07159 A3

(51) International Patent Classification[7]: C12Q 1/68, G01N 35/08, B01L 7/00, 3/00

(21) International Application Number: PCT/IB00/01137

(22) International Filing Date: 28 July 2000 (28.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

99/09806	28 July 1999 (28.07.1999)	FR
99/11652	17 September 1999 (17.09.1999)	FR
99/12317	1 October 1999 (01.10.1999)	FR

(71) Applicants *(for all designated States except US)*: **GENSET** [FR/FR]; Intellectual Property Department, 24, rue Royale, F-75008 Paris (FR). **COMMISSARIAT A L'ENERGIE ATOMIQUE** [FR/FR]; 31-33, rue de La Federation, F-75015 Paris (FR).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **FOUILLET, Yves** [FR/FR]; Chemin des Carrieres, Le Chevalon de Voreppe, F-38340 Voreppe (FR). **VAUCHIER, Claude** [FR/FR]; 2, impasse Lartigues, F-38120 Saint-Egreve (FR). **CLERC, Jean-Frederic** [FR/FR]; 8, rue du Mont Perthuis, Le Fontanil-Cornillon, F-38120 Saint-Egreve (FR). **PEPONNET, Christine** [FR/FR]; 5, square des Sarcelles, F-91250 Tigery (FR).

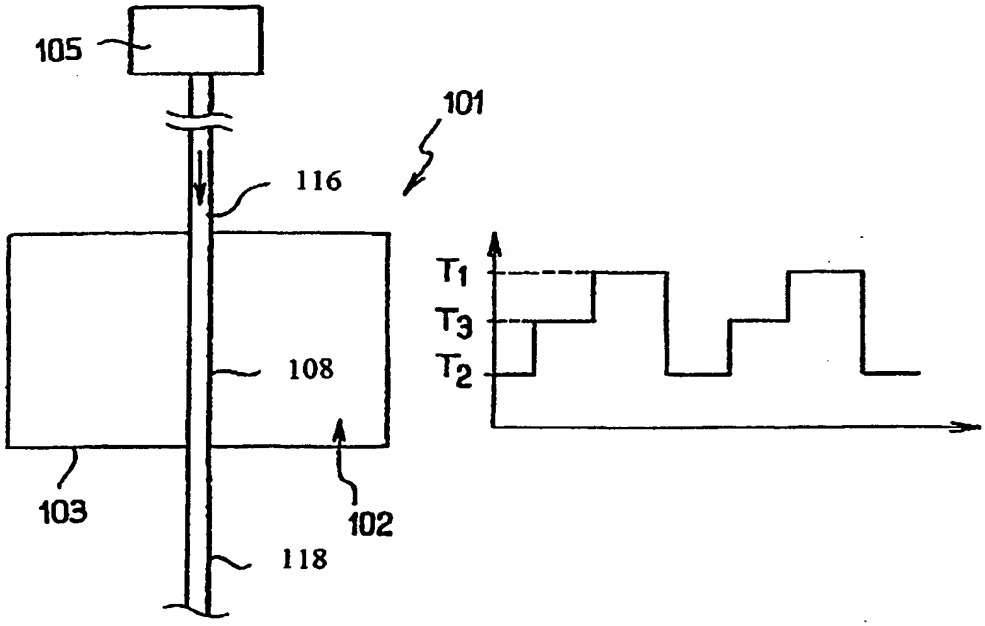
(74) Common Representative: **GENSET**; Intellectual Property Department, 24, rue Royale, F-75008 Paris (FR).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,

[Continued on next page]

(54) Title: INTEGRATION OF BIOCHEMICAL PROTOCOLS IN A CONTINUOUS FLOW MICROFLUIDIC DEVICE



(57) Abstract: Provided is a microfluidic device comprising a microfluidic substrate comprising at least one pathway for sample flow; and at least one thermal transfer member which is capable of cycling between at least two temperatures. The thermal transfer member is adapted to heat at least a portion of the sample pathway while a sample is flowing along said at least a portion of said sample pathway. Provided also are methods of carrying out biochemical protocols using such a device.

WO 01/07159 A3

IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

(88) Date of publication of the international search report:
25 May 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PC IB 00/01137

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 G01N35/08 B01L7/00 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 325 464 A (BRUKER FRANZEN ANALYTIK GMBH) 25 November 1998 (1998-11-25) cited in the application abstract; claims 1-10; figures 1-4 page 7, line 6 - line 30 page 9, line 7 -page 10, line 28 page 11, line 7 - line 28 page 13, line 3 -page 14, line 24 --- -/--	1-40

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 November 2000	15.02.01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	HOCQUET, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PC IB 00/01137

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category ˇ	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KOPP ET AL: "chemical amplification:continuous flow PCR on a chip" SCIENCE,US,AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 280, no. 280, 15 May 1998 (1998-05-15), pages 1046-1048-1048, XP002107956 ISSN: 0036-8075 page 1046; figure 1B	1-40
P,X	WO 00 23190 A (CLERC JEAN FREDERIC ;COMMISSARIAT ENERGIE ATOMIQUE (FR); FOUILLET) 27 April 2000 (2000-04-27) page 3, line 10 - line 22 page 5, line 10 - line 17 page 5, line 23 - line 28 page 11, line 18 - line 22 page 13, line 10 - line 22	22-26,28
P,A	page 14, line 6 - line 12; figure A page 19, line 10 - line 15	12
A	EP 0 636 413 A (PERKIN ELMER CORP) 1 February 1995 (1995-02-01)	1
X	column 13, line 38 -column 14, line 10; figure 2	22
Y,P	WO 99 41015 A (POSER SIEGFRIED ;SCHULZ TORSTEN (DE); INST PHYSIKALISCHE HOCHTECHN) 19 August 1999 (1999-08-19) page 5, line 12 - line 32; figures	22
Y	WO 96 15269 A (UNIV PENNSYLVANIA) 23 May 1996 (1996-05-23) page 25, line 17 - line 27; figures page 37, line 16 -page 38, line 29; figures 19-22 page 48, line 24 - line 25; figure 10 page 49, line 33 -page 50, line 6; figure 10 page 49, line 30 - line 32; figure 10	22
A	US 5 270 183 A (CORBETT JOHN M ET AL) 14 December 1993 (1993-12-14) column 6, line 20 - line 24 column 8, line 58 - line 62; figures 1,2	12,15
P,A	WO 99 39005 A (MAYO FOUNDATION ;UNIV PITTSBURGH (US)) 5 August 1999 (1999-08-05) the whole document	1
A	US 5 866 345 A (WILDING PETER ET AL) 2 February 1999 (1999-02-02) the whole document	1

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 00/01137

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-40

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-40

   devices and methods for thermocycling samples flowing continuously along channels

2. Claims: 41-51

   process for detecting or identifying in continuous flow nucleotides using microsequencing reagent

INTERNATIONAL SEARCH REPORT

formation on patent family members

International Application No
PC . iB 00/01137

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2325464 A	25-11-1998	DE 19717085 A	05-11-1998
WO 0023190 A	27-04-2000	NONE	
EP 0636413 A	01-02-1995	JP 7075544 A	20-03-1995
		US 6033880 A	07-03-2000
		US 5720923 A	24-02-1998
		US 5827480 A	27-10-1998
		US 5779977 A	14-07-1998
WO 9941015 A	19-08-1999	EP 1054735 A	29-11-2000
WO 9615269 A	23-05-1996	US 5587128 A	24-12-1996
		US 5744366 A	28-04-1998
		US 5726026 A	10-03-1998
		AU 704277 B	15-04-1999
		AU 4236996 A	06-06-1996
		AU 698213 B	29-10-1998
		AU 4282896 A	06-06-1996
		AU 4282996 A	06-06-1996
		CA 2181189 A	23-05-1996
		CA 2181190 A	23-05-1996
		CN 1157639 A	20-08-1997
		EP 0739240 A	30-10-1996
		EP 0739423 A	30-10-1996
		JP 9511407 T	18-11-1997
		JP 9509498 T	22-09-1997
		WO 9614933 A	23-05-1996
		WO 9614934 A	23-05-1996
		CN 1143917 A	26-02-1997
		US 5928880 A	27-07-1999
US 5270183 A	14-12-1993	AU 660652 B	06-07-1995
		AU 1185092 A	07-09-1992
		WO 9213967 A	20-08-1992
WO 9939005 A	05-08-1999	AU 2347799 A	16-08-1999
		AU 2479199 A	16-08-1999
		EP 1051518 A	15-11-2000
		WO 9939120 A	05-08-1999
US 5866345 A	02-02-1999	US 5637469 A	10-06-1997
		AT 155711 T	15-08-1997
		AT 167816 T	15-07-1998
		AT 140025 T	15-07-1996
		AT 140880 T	15-08-1996
		AT 174813 T	15-01-1999
		AU 677780 B	08-05-1997
		AU 4222393 A	29-11-1993
		AU 680195 B	24-07-1997
		AU 4222593 A	29-11-1993
		AU 677781 B	08-05-1997
		AU 4222693 A	29-11-1993
		AU 4222793 A	29-11-1993
		AU 677197 B	17-04-1997
		AU 4223593 A	29-11-1993
		CA 2134474 A	11-11-1993
		CA 2134475 A	11-11-1993

INTERNATIONAL SEARCH REPORT

formation on patent family members

International Application No
PC, IB 00/01137

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5866345 A		CA 2134476 A	11-11-1993
		CA 2134477 A	11-11-1993
		CA 2134478 A	11-11-1993
		DE 69303483 D	08-08-1996
		DE 69303483 T	06-02-1997
		DE 69303898 D	05-09-1996
		DE 69303898 T	20-02-1997
		DE 69312483 D	04-09-1997
		DE 69312483 T	12-02-1998
		DE 69319427 D	06-08-1998
		DE 69319427 T	10-12-1998
		DE 69322774 D	04-02-1999
		DE 69322774 T	17-06-1999
		EP 0637996 A	15-02-1995
		EP 0637997 A	15-02-1995
		EP 0639223 A	22-02-1995
		EP 0637998 A	15-02-1995
		EP 0637999 A	15-02-1995
		ES 2106341 T	01-11-1997
		ES 2127276 T	16-04-1999
		GR 3025037 T	30-01-1998
		GR 3029509 T	28-05-1999
		HK 16897 A	13-02-1997
		JP 7506430 T	13-07-1995
		JP 7506431 T	13-07-1995
		JP 7506256 T	13-07-1995
		JP 7506257 T	13-07-1995
		JP 7506258 T	13-07-1995
		WO 9322053 A	11-11-1993
		WO 9322054 A	11-11-1993
		WO 9322421 A	11-11-1993
		WO 9322055 A	11-11-1993
		WO 9322058 A	11-11-1993